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In the Supreme Court of the United States

OCTOBER TERM, 1964.

No. 701.

DR. HENRY TURKEL and UBIOTICA CORPORATION,
Petitioners,

v.

FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
Respondent.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE SIXTH CIRCUIT.

PETITIONERS' REPLY BRIEF.

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PETITIONERS' REPLY BRIEF.

Petitioners, under and by virtue of the provisions of Rule 24 of this Court, herewith present this Reply Brief directed to the Brief of the United States in Opposition heretofore filed.

OPINION BELOW.

The opinion of the Court of Appeals (Pet. App. 12) is reported at 334 F. 2d 844.

JURISDICTION.

The judgment of the Court of Appeals was entered on July 21, 1964. A petition for rehearing was denied on September 14, 1964. The Petition for a Writ of Certiorari was filed on November 18, 1964. The Brief for the United States in Opposition was filed on December 18, 1964. The jurisdiction of this Court is invoked under 28 U. S. C. 1254(1).

QUESTIONS PRESENTED.

In a suit filed under the provisions of 21 U. S. C. 355-(h), providing for a Petition to Review an order withdrawing approval of an application granting an exemption for the investigational use of a drug, the Court of Appeals for the Sixth Circuit granted the Respondent's Motion to Dismiss said Petition to Review. The Court of Appeals stated in its decision that there was no recourse available to the Petitioners to review the order of the Food and Drug Administration, issued against the Petitioners. The Court of Appeals further made a finding that a tendered record of the Food and Drug Administration could not be received by the Court for its consideration in connection with the issues presented in this cause. The questions presented are:

1. Whether the 1962 Amendments to the Food and Drug Act that the right of appeal to the United States Court of Appeals granted by 21 U. S. C., Section 355(h), applied to an order of the Secretary, Health, Education and Welfare Department, withdrawing approval of an investigational exemption granted permitting the distribution of a drug for investigational use.

2. Whether Section 262 of the Judicial Code grants jurisdiction to federal courts to review an order of the Secretary, Health, Education and Welfare Department, withdrawing approval of an investigational exemption granted permitting the distribution of a drug for investigational use.

3. Whether the Due Process Clause of the Fifth Amendment of the U. S. Constitution protects against unreasonable and unwarranted conditions imposed

by regulations adopted by a federal agency under a directive contained in an Act of Congress.

4. Whether the Due Process Clause of the Fifth Amendment of the U. S. Constitution protects against an unreasonable and unwarranted interference in the investigational use of a drug, when all of the medical evidence available with respect to the investigational use of said drug indicates that the same is devoid of harmful effects, and beneficial to those patients being administered the same.

5. Whether the Due Process Clause of the Fifth Amendment of the U. S. Constitution protects against a proceeding, where an investigational use exemption is withdrawn by the Food and Drug Administration, without a hearing, without confrontation, and without an opportunity to present evidence germane to the subject matter, before such time as a final order of the Food and Drug Administration is issued with respect to the termination of the investigational use exemption in existence.

6. Whether the Due Process Clause of the Fifth Amendment of the U. S. Constitution protects duly licensed physicians against the unbridled and arbitrary use of power by the Food and Drug Administration in refusing to present and disclose reasons upon which is premised an order of termination of an existing exemption authorizing the investigational use of a drug.

7. Whether the Due Process Clause of the Fifth Amendment of the U. S. Constitution requires a judicial review of proceedings conducted by a federal agency, wherein said federal agency denies a hearing,

confrontation and findings before a final order is issued to Petitioners.

In the Brief for the United States in Opposition, under the subtitle "Questions Presented," paragraph 2 (Resp. Brief 2), the following appears:

> "2. Whether the judgment of the court of appeals dismissing petitioners' appeal for lack of jurisdiction violated petitioners' right to due process under the Fifth Amendment to the Constitution."

This question is not directly involved in this case, nor is this question invoked, by the Petitioners. Rather the question propounded, in relation to the guarantees of the Fifth Amendment to the Constitution are whether the said Amendment protects against

> (a) "* * * unreasonable and unwarranted conditions imposed by regulations adopted by a federal agency, under a directive contained in an Act of Congress," or
>
> (b) "* * * an unreasonable and unwarranted interference in the investigational use of a drug, when all of the medical evidence available with respect to the investigational use of said drug indicates that the same is devoid of harmful effects, and beneficial to those patients being administered the same," or
>
> (c) "* * * a proceeding, where an investigational use exemption is withdrawn by the Food and Drug Administration, without a hearing, without confrontation, and without an opportunity to present evidence germane to the subject matter, before such time as a final order of the Food and Drug Administration is issued with respect to the termination of the investigational use exemption in existence."

And whether the said Amendment

> (d) "* * * protects duly licensed physicians against the unbridled and arbitrary use of power by

the Food and Drug Administration in refusing to present and disclose reasons upon which is premised an order of termination of an existing exemption authorizing the investigational use of a drug," and

(e) "* * * requires a judicial review of proceedings conducted by a federal agency, wherein said federal agency denies a hearing, confrontation and findings before a final order is issued * * *."

CONSTITUTION, STATUTES, FEDERAL RULES AND REGULATIONS INVOLVED.

Involved herein are the following: Amendment V, U. S. Constitution, set forth in the Appendix (Pet. App. 18); Federal Food, Drug and Cosmetic Act, as amended, 21 U. S. C. 355, set forth in the Appendix (Pet. App. 19-27); Regulations adopted by the Food and Drug Administration, 28 Federal Register, 170-182, 319, 5048 (21 C. F. R. 130.3), set forth in the Appendix (Pet. App. 27-48); and Rules 26 and 33 of the Federal Rules of Civil Procedure.

SUPPLEMENTAL STATEMENT.

The Petitioners, the Court of Appeals, and this Court, are seriously handicapped at this point, because of the fact that the Respondent, Food and Drug Administration, has not placed in the Record, and has not been required to file in the Record, all material, writings, documents, communications and other indicia of evidence, with respect to its evaluation of the "U" Series Drugs.

However, the Petitioners have in their possession, copies of some of the writings of the Respondent, with respect to its actions and attitudes toward the "U" Series Drugs; and there is attached hereto the following:

Exhibit 1A. This is a reproduction of a letter issued by the Respondent by its Medical Officer, Divi-

sion of New Drugs, Bureau of Medicine, one Jean D. Lockhart, M. D., addressed to the Petitioners, dated August 2, 1963, which states in part as follows:

> *"In summary, there is no basis for considering that the random, empirical and scientifically irrational choice of drugs and dosages contained in this NDA is either safe or effective in the management of Mongolism. It is our opinion that it may be impossible to write suitable labeling for efficacy for this product;* **in view of the cytogenetic basis of Mongolism, we recommend that you abandon work on this application."** (Emphasis added.)

Exhibit 2A. This is a reproduction of a letter transmitted by Richard L. Masland, M. D., Director, National Institute of Neurological Diseases and Blindness, National Institutes of Health, to Hon. John E. Fogarty, M. C., dated March 3, 1964, which states in part as follows:

> *"The drugs included in Dr. Turkel's "U Series" are well-known compounds. On theoretical grounds, and based on the known effects of these drugs, which consist of vitamins, minerals, and other medications, our advisors have stated that, although they are not harmful, they doubt the drugs would be of specific value in treating mongolism. However, because of Dr. Turkel's claims, both Dr. Bailey, former Institute director, and I have met with him to discuss his treatment and the type of results he has observed in treated patients. The Institute has also tried, without success to find investigators willing to devote the time required to the scientific evaluation of the Turkel therapy."*

Petitioners have labored since 1943 in the development of the "U" Series Drugs, which are directed toward treatment of the condition resulting from inborn error metabolism. (Exhibits 3A and 4A.)

Hence we reiterate that the opinion and judgment of the Court of Appeals in effect held that there is no protection to the Petitioners in this case, where all of the procedural requirements of due process were ignored and denied by the arbitrary, unwarranted and summary action of the Food and Drug Administration.

REASONS FOR GRANTING THE WRIT.

Petitioners respectfully incorporate by reference the statements made under this heading heretofore (Pet. App. 7-10).

CONCLUSION.

For the reasons set forth above, supplementing those contained in the Petitioners' Application, it is respectfully submitted that the Petition for a Writ of Certiorari should be granted.

LEO E. RATTAY,
Counsel for Petitioners.

EXHIBIT 1A.

DEPARTMENT OF

HEALTH, EDUCATION, AND WELFARE

FOOD AND DRUG ADMINISTRATION

Washington 25, D. C.

NDA 14-712

Aug. 2, 1963

Ubiotica Corporation
Attention: Dr. Henry Turkel
8000 West Seven Mile Road
Detroit 21, Michigan

Gentlemen:

Reference is made to your new drug application dated May 29, 1963 submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for the preparation "'U' Series Drugs."

The application is incomplete under section 505(b)(1) and (6) as follows:

No scientific evidence is supplied that these drugs have altered the mongoloid condition of the children who are treated. No diagnostic studies are documented. Laboratory work is conspicuous by its absence. For example, there is no way of determining the original thyroid status of children who are being treated with thyroglobulin and tri-iodothyronine. Metrazol is used as one component of the Series although electroencephalograms are never mentioned in the NDA. At least four of the 15 "Investigators" for the drug are not medical doctors, and it is evident that the others are not bone fide investigators in any scientific sense but merely agents who administer the drug. No rationale is given for the choice of the 51 component ingredients of this "Series" or their dosages. No evidence is offered that mongoloid patients have nutritional or hormonal requirements different from normal subjects. No recognition is made of the cytogenetic basis of mongolism.

In summary, there is no basis for considering that the random, empirical and scientifically irrational choice of drugs and dosages contained in this NDA is either safe or effective in the management of Mongolism. It is our opinion that it may be impossible to write suitable labeling for efficacy for this product; *in view of the cytogenetic basis of Mongolism, we recommend that you abandon work on this application.*

The application is not approvable in accordance with section 130.5(a) of the New Drug Regulations, and may not be filed since it is incomplete on its face in that it does not contain all the matter required by sections 505(b)(1), (2), (3), (4), (5) and (6) of the Act.

Since the application is incomplete under section 505 (b)(1), (2), (3), (4), (5) and (6) of the Act, it may not be filed as an application provided for in section 505(b).

Sincerely yours,

JEAN D. LOCKHART, M.D.
Medical Officer
Division of New Drugs
Bureau of Medicine

EXHIBIT 2A.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
Bethesda 14, Md.

Mar. 3, 1964.

Dear Mr. Fogarty:

This is in reply to your request for comment on the letter of Mr. and Mrs. Ervin Ronell of Elk Point, South Dakota, concerning the use of the "U Series" of drugs for the treatment of mongolism (Down's syndrome).

From time to time, as I am sure you know, various special diets and supplementary materials have been reported beneficial for mongoloid children. Research studies to date, however, have not demonstrated that such treatment is of specific value for this disorder.

Experience has shown repeatedly that the performance of the mongoloid child is significantly influenced by active encouragement, attention, and good general care. Many of the reputed effects of specific treatment have subsequently been shown to result from the nonspecific stimulation which the treated child received from those interested in observing the results of therapy.

The drugs included in Dr. Turkel's "U Series" are well-known compounds. On theoretical grounds, and based on the known effects of these drugs, which consist of vitamins, minerals, and other medications, our advisors have stated that, *although they are not harmful,* they doubt the drugs would be of specific value in treating mongolism. However, because of Dr. Turkel's claims, both Dr. Bailey, former Institute director, and I have met with him to discuss his treatment and the type of results he has observed in treated patients. *The Institute has also tried, without success to find investigators willing to devote the time required to the scientific evaluation of the Turkel therapy.*

A recently completed independent study in Buffalo on the "U Series" drugs revealed no improvement in 12 children treated with the Series for a 1-year period. I am enclosing a copy of the report on this investigation as published in the Journal of the American Medical Association, February 1, 1964.

Of course, as you are aware, licensing and distribution of the Turkel drugs is under the authority of the Food and Drug Administration, in compliance with the drug-testing provisions of the law. As I understand, the U-Series medication may be distributed to qualified medical investigators for bona fide clinical study at any time. FDA, I am sure, can provide you with other information in this matter.

I hope these comments will prove useful to you. Please let us know if we can be of further help.

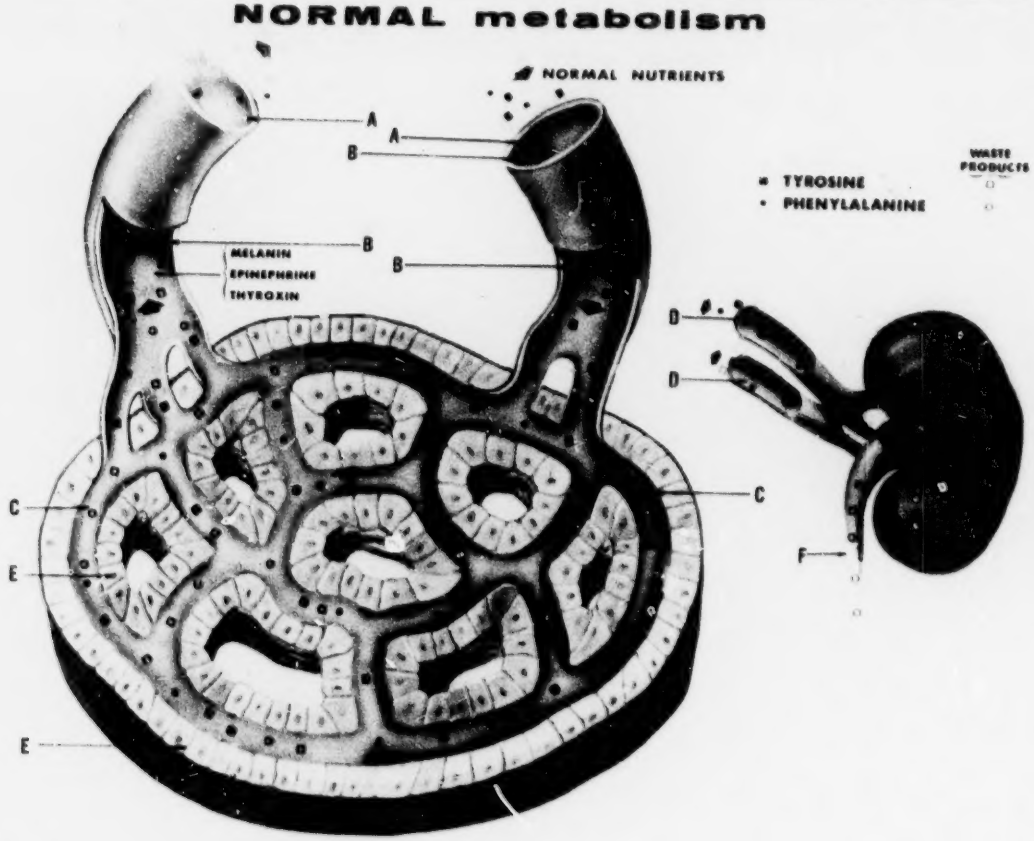
Sincerely yours,

RICHARD L. MASLAND, M.D.
Director, National Institute of Neurological Diseases and Blindness

Honorable John E. Fogarty
House of Representatives
Washington, D. C. 20515

Enclosure

EXHIBIT 3A.



NORMAL METABOLISM

A—Potential space for circulating blood, nutrients, hormones, waste products, etc.

B—Arteries and veins NOT blocked by harmful metabolites.

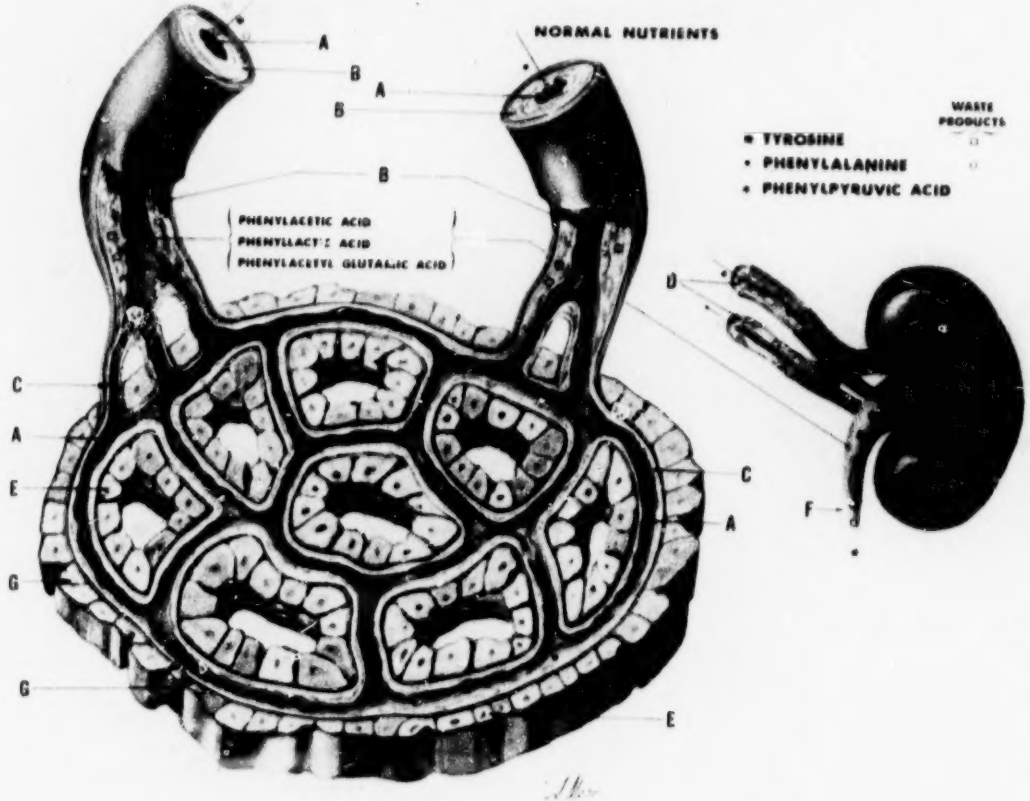
C—Arteries and veins within organs and tissues NOT blocked by harmful metabolites.

D—Renal arteries and veins NOT blocked by harmful metabolites.

E—Organs and tissues grow, mature and function at normal rate in a "timely" manner.

F—Urine contains normal waste products.

INBORN ERROR metabolism



BY HENRY TURKEL 1964

INBORN ERROR METABOLISM

A—Less space available for circulating blood, nutrients, hormones, waste products, etc.

B—Arteries and veins BLOCKED by harmful metabolites.

C—Arteries and veins within organs and tissues BLOCKED by harmful metabolites.

D—Renal arteries and veins are BLOCKED by harmful metabolites.

E—Organs and tissues grow, mature and function at lower rate as result of receiving an insufficient amount of nutrients, etc.

F—Urine contains fewer normal products plus unmetabolized normal and alternate metabolites and their abnormal products.

G—Organs and tissues deprived of nutrients, hormones, etc., as well as affected by harmful metabolites grow, mature and function at a lower rate and untimely manner with resultant inborn structural anomalies characteristic of inborn errors of metabolism, e.g. mongolism, arteriosclerosis, phenylketonuria, etc.

EXHIBIT 4A.